Herbal Medicine and Oral Health: A Review

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How to cite the article:

Abstract:
Medicinal plants have been used since ancient times for the treatment of different diseases. Natural sources are one of the important fields of research for preventing immunological complications. Using herbal medicine has decreased as the result of the development of chemical drugs. This review aimed to study herbal medicine regarding the oral cavity. English literature was searched with the terms “herbal medicine and oral cavity” in two data bases of PubMed, and Google scholar among published studies from 2000 to 2015. All review articles, original articles, case reports, and case series were evaluated. This study found that many herbs are used in the treatment of diseases, among which many do not have any side effects. Herbal medicine is a complementary/alternative effective therapy for several diseases. Despite the development of many chemical drugs, using herbal medicine is highly demanded.

Key Words: Disease, herbal medicine, mouth, neoplasm

Introduction
Medicinal plants have been used since ancient times for the treatment of different diseases.1 Natural sources are one of the important fields of research for preventing immunological complications.2 The use of herbal medicine had decreased as the result of the development of chemical drugs. However, many scientists are still using herbal medicines in different fields.3 For example, the bark of Prunus yedoensis which belongs to Rosaceae family is used for the treatment of skin inflammatory lesions. It can decrease the serum levels of tumor necrosis factor-a and interleukin-6 (IL-6) in macrophages in mice.4 In addition, rhizoma Acori tatarinowii has been applied to patients with cognitive deficits caused either by aging or by neurodegenerative diseases including Alzheimer’s disease.5 Herbal products have also been proposed as adjuvant therapy of diseases such as cardiovascular diseases, cancer, diabetes mellitus in which free radicals play a key role in their pathogenesis.6 There are some reports on Korean medicine therapy to treat different types of cancer such as metastatic bladder cancer in both lungs without chemotherapy or radiotherapy.7 The metastatic and angiogenic potential of Anisi stellate fructus extract were examined in in vitro and in vivo studies. The results showed that it remarkably reduced the number of pulmonary metastatic colonies in mice and also suppressed in vivo tumor-induced angiogenesis through a reduction of pro-angiogenic factors in tumors.8 One of the traditional herbal medicines is Guibitang, which induces apoptotic death in colon cancer cells by regulating the activities of mitogen-activated protein kinases. Furthermore, Guibitang stimulates MAPks and pS3 signaling pathways that are required for cell growth and tumorigenesis.9 Interestingly, stem cells from human exfoliated deciduous teeth differentiate into functional hepatocyte-like cells by herbal medicine such as liquorice or angelica extracts.10

Oral health has a great impact on the general quality of life, and poor oral health has a great impact on chronic conditions and systemic diseases. In the oral cavity, herbal medicine has been used for the treatment of several diseases.11 More than 700 bacterial species have been detected in the oral cavity.12 Some of these bacteria have been implicated in oral diseases such as caries and periodontitis.13 Biofilm bacteria have increased antimicrobial resistance and, for this reason, new antimicrobials are highly demanded.14 Herbal medicine can be used in the treatment of several oral diseases. In addition, herbal remedies are used as homeopathic drugs, alternative therapy, in oral diseases such as ulcer, lichen planus, and xerostomia.15

Materials and Methods
English literature searched with the terms “herbal medicine and oral cavity” in two data bases of PubMed, and Google scholar among published studies since 2000 to 2015. All related review articles, original articles, case reports, and case series were evaluated.

Results

Oral epithelium
Oral epithelium is a barrier against microbial infection by producing antimicrobial peptides which function against bacteria, fungi, and viruses.16 Hangeshashinto (HST), a traditional Japanese herbal medicine, has anti-inflammatory effects. In the oral cavity, HST may increase immunity by up-regulation of calprotectin, a heterodimer of S100A8 and S100A9 with antimicrobial properties, which is expressed in gingival keratinocytes.17 18
**Oral microbiome**

In the human oral cavity, micro-organisms have been referred to as the oral microflora, oral microbiota, or more recently as the oral microbiome. The term microbiome was created by Joshua Lederberg. In the mouth, there are several microbial habitats including teeth, gingival sulcus, attached gingiva, tongue, lip, hard palate, and soft palate. Some *Plantago* species have considerable antibacterial, anti-inflammatory, and antioxidant activities. *Plantago lanceolata* infusion has antimicrobial activity, particularly against salivary streptococci. Thus, it is a natural anti-cariogenic agent. Herbal products of *Persica* inhibit the growth of *Porphyromonas gingivalis* and *Aggregatibacter actinomycetemcomitans* in *in vitro* study. Clove and gallnut extracts have antibacterial activity on *Streptococcus mutans* and *Streptococcus salivarius*. Propolis is the generic name for the resinous substance produced by honeybees (*Apis mellifera*) and has been used for medicinal purposes as it has antimicrobial, antitumoral, and immunomodulatory properties. *Baccharis dracunculifolia* is the most important botanical source of Southeastern Brazilian propolis which reduces the rate of plaque (biofilm) in the same level as chloride tricoslan.

**Dental caries**

Dental caries is a very common infectious oral disease which is associated with various pathogenic micro-organisms most probably *S. mutans*. It has this ability to produce glucosyltransferases, insoluble glucans, and acids. Bacterial plaque is a general term and refers to the accumulation of microorganisms (mainly bacteria) and plays a primary role in the development of dental caries and periodontal disease. It is suggested that *Streptococcus sanguinis* is the first responsible for formation and maturation of bacterial plaque, and *S. salivarius* is a common micro-organism in the saliva and on oral mucosal surfaces especially on the dorsum of tongue, buccal mucosa. The cariogenic properties of *S. mutans* and *S. salivarius* result in the production of insoluble glucans from sucrose which adheres to tooth surfaces and have acidogenicity properties. *Rhus coriaria* L. is a commercially available species of Sumac and its water extract reduces bacterial biofilm formation on orthodontic wire. Emodin is a natural anthraquinone derived from the roots and rhizomes of a number of plants including *Rheum undulatum* and *Polygonum cuspidatum* markedly suppresses the production of acid and insoluble glucan by *S. mutans* in rats. This finding suggests that emodin may be responsible for the anti-cariogenic activity of *R. undulatum* and *P. cuspidatum*.

**Gingivitis and periodontitis**

Biofilm is a dense non-calciﬁed mass composed of micro-organisms mainly *Streptococcus mitis* and *Streptococcus sanguis*. Mechanical and chemical oral hygiene methods control dental biofilm. Pomegranate and chamomile plant extracts in the form of mouth rinse reduce the gingival bleeding. Chamomile has analgesic, antioxidant, antiparasitic, anticancer and immunoregulatory properties, and therefore, can be used to treat some inflammatory diseases such as gastrointestinal and skin diseases. *Punica granatum* (pomegranate) also has a potential to prevent and fight several inflammatory and microbial diseases. Rokumigan, a Kampo Japanese traditional medicine made of six different plants, prevents biofilm formation by *Fusobacterium nucleatum*, inhibits IL-6 and IL-8 secreted by mucosal cells, and promotes wound healing in a fibroblast model. These properties make it an attractive candidate for prevention and treatment of periodontitis. A previous study showed that sword bean extract containing 6.4% canavanine inhibits the growth of *P. gingivalis* and *Fusobacterium nucleatum* in rats. Therefore, alveolar bone resorption can be inhibited using sword bean extract. The hydrophobic gingiva-adhering gel has the same effect of chlorhexidine after scaling and root planning. Thus, it is a suitable alternative treatment for moderate periodontitis in the patients which are allergic to chlorhexidine.

**Oral diseases**

Hand, foot, and mouth disease (HFMD) is a common infectious disease in children usually caused by enterovirus 71 or coxsackievirus type A 16. The combination of conventional therapy with Ji Jinliangngre Efervescent tablets signiﬁcantly reduces the fever clearance time and healing time of skin or oral mucosal lesions without any adverse event and complications. Reduning injection, composed of three herbs (Herba Artemisia annua, Lonicera japonica Thumb, and *Gardena jasminoides* Ellis) reduces the fever and inflammation associated with HFMD. However, it is not useful in the treatment of severe HFMD cases. Jinzheng oral liquid is a kind of Chinese patent medicine extracted from the herbs including Baikal skullcap root, rhubarb, and gypsum. It has been used to treat fever in some viral infections in children. Jinzheng oral liquid improves the clinical symptoms of HFMD including fever, oral ulcers, and vesicles on hand or foot, and other symptoms in multiple organs or systems.

Oral submucous fibrosis is a high-risk premalignant condition of the oral cavity, pharynx and upper digestive tract which is characterized by progressive inability to open the mouth and also by inflammation and progressive fibrosis of submucosal tissues. Oxitard, an herbal antioxidant containing the extracts of *Mangifera indica*, *Withania somnifera*, *Daucus carota*, *Glycyrrhiza glabra*, *Vitis vinifera*, powders of *Emulba ofﬁcinalis*, and *Yashada bhasma*; oils of *Triticum aestivum* can signiﬁcantly improve clinical symptoms of oral submucous fibrosis.

Aphthous stomatitis is a very common oral painful ulcerative lesion. Ginger, a native eastern Indian medicinal plant with anti-inflammatory effect, has been used for the treatment of aphthous stomatitis. A significant decrease in the severity of pain, in the diameter of inflammatory zone has been
observed after treatment with mucoadhesive containing ginger.\textsuperscript{57} Chamomilla tincture, a herbal medicine, has anti-inflammatory and analgesic, anti-spasm, anti-bacterial, and fungal effects.\textsuperscript{58} Chamomilla mouth rinse is effective in the treatment of recurrent aphthous stomatitis in rats by controlling the pain and burning sensation without producing any adverse side effects.\textsuperscript{46} Quercetin, an antioxidant, has been used in the treatment of different systemic and oral lesions like aphthous ulcers\textsuperscript{42,43} but has no effect on the treatment of oral lichen planus.\textsuperscript{44} Zeng Ye decoction extracted from figwort, Ophiopogon japonicus, and Rehmannia glutinosa Libosch has a significant therapeutic effect on primary Sjogren’s syndrome through up-regulation of the levels of aquaporin −1 and −5, integral membrane pore proteins.\textsuperscript{45} Dry mouth is a common complication of radiotherapy for head and neck cancer.\textsuperscript{46} Malva sylvestris L and Alcea digitata (Boiss) Alef is traditional Persian medicine which has antitussive, antioxidant, expectorant, anti-inflammatory, antimicrobial, and laxative therapeutic properties.\textsuperscript{47} These herbs can decrease the grade of dry mouth in patients who received radiotherapy due to cancer in the head and neck area.\textsuperscript{48} Cis-platinum (II) diammine dichloride is an anticancer agent, and can be used for cancer therapy but has serious side-effects, including xerostomia. To reduce the adverse effect of chemotherapy on salivary gland function, some additional drugs are needed.\textsuperscript{49} Two Chinese medical herbal extracts from the root barks of Juncus effusus and Paeonia suffruticosa protect salivary gland acinar cells from apoptosis. Hence, they can be attractive alternative drugs to prevent Cis-platinum caused xerostomia.\textsuperscript{50}

After mumps, Juvenile recurrent parotitis (JRP) is the second most common infectious salivary gland disease during childhood. Huangqi granule is a preparation of an extract of Radix astragali, a Chinese traditional medicine, and completely treats the JRP patients with a significant reduction of average recurrence frequency.\textsuperscript{51}

**Oral cancer**

Oral squamous cell carcinoma (SCC) comprises 90% of all head and neck cancers which has a poor prognosis.\textsuperscript{52} Chemotherapy is suggested therapy for advanced stages of the disease, but resistance of cancer cells to chemotherapy drugs limits the efficiency of chemotherapy.\textsuperscript{53} Herbal medicine has been shown to offer protection against different cancers.\textsuperscript{54-56} In Asian countries, herbal medicine is used to treat a variety of diseases. Some advanced diseases such as cancers require multi-targeting treatment. Synergy of herbs has a better therapeutic efficacy than that of a single herb.\textsuperscript{57} Pterostilbene has been identified in several plants of the genus Pterocarpus and has antioxidant activity, and therefore, can inhibit DNA synthesis.\textsuperscript{58} Pterostilbene induces apoptosis of oral cancer cells via activation of caspase-3, -8, and -9. Pterostilbene also induces autophagy on human oral cancer cells through modulation of Akt and mitogen-activated protein kinase pathway.\textsuperscript{59} Grape seed extract (V. vinifera) induces apoptosis in oral SCC.\textsuperscript{60} Insect tea a natural organic tea has a preventive effect on the buccal mucosa cancer in mice via inducing apoptosis.\textsuperscript{61} Iranian orthodox black tea extracts and hydro melanolic purified fractions (40%, 60%, 80% and 100%) induce apoptosis in oral cancer cells in vitro.\textsuperscript{62} Scutellariae radix is one of the most widely used anticancer herbal medicines in several Asian countries induces apoptosis in chemo-resistant human tongue cancer cells.\textsuperscript{63} The dried root of Saussurea lappa Dance which has been traditionally used for abdominal pain in Asia inhibits oral cancer cell proliferation via apoptosis pathway.\textsuperscript{64} A previous study on adenoid cystic carcinoma indicated that intratumoral high-dose injections of ABNOBAviscum Quercus and ABNOBAviscum FraxiniViscum album extracts which are endotoxin-free plant extracts from European Viscum album extract could decrease the size of tumor without any side effects such as fever, local inflammation, swelling, and pain.\textsuperscript{65} Although low-dose adjunct VAE treatment has shown any side effect on head and neck cancer patients, cytotoxic effects of VAE have been observed in head and neck SCC cell lines.\textsuperscript{66} Table 1 summarizes the effect of herbal medicine in oral health.

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<th>Oral epithelium</th>
<th>Oral microbiome</th>
<th>Dental caries</th>
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<td>Rhus coriaria L.</td>
<td>Pomegranate extract (P. granatum)</td>
<td>Jinlianqingre Effervescent</td>
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<td>Canavanine</td>
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<td>Huangqi granule</td>
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</table>

**Table 1:** The effect of herbal medicine in oral health.
Discussion
Herbal medicine is a complementary/alternative effective therapy for several diseases. Despite the development of many chemical drugs, the use of herbal medicine is highly demanded. Although some allergic reactions and adverse side effects have been reported, they can still be used to treat diseases. If there will be some proof for therapeutic effects of herbal medicine for the treatment of serious diseases, especially cancers, they can be used as alternative or adjuvant drugs. It is worthy to note that not always herbal medicine has therapeutic effects. There are a few reports indicating some allergic reactions or adverse side effects for herbal medicine. For instance, developing hepatitis and Sjogren's syndrome after taking some unknown herbal medicine,65 or inducing plasma cell gingivitis after using toothpaste containing Acacia have been reported.66 In addition, inducing hand-foot syndrome after topical use of henna toothpaste containing Acacia have been reported.67 In addition, inducing hand-foot syndrome after topical use of henna ameliorated,66 and developing Stevens–Johnson syndrome due to unknown Indian herbs is some other adverse side effects.70

Conclusion
In conclusion, herbal medicine is an alternative therapy which is effective in some cases especially those with failure treatment with conventional drugs. More investigation should be done to evaluate the effectiveness of herbal medicine.

Acknowledgments
This study was supported by Hamadan University.

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